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EXAMINER

HM22/0906

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1655
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09/06/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/530,772

Applicant(s)

Brahmbhatt

Examiner

Arun Chakrabarti

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Aug 21, 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 13-19 is/are rejected.
- 7) ☒ Claim(s) 8-12 is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

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DETAILED ACTION

Specification

1. Claims 8-12 are objected to under 37 CAR 1.75© as being in improper form because a multiple dependent claim cannot depend on another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 8-12 have not been further treated on the merit

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 15-19 are rejected as being indefinite because the instantly claimed methods lack a final process step that clearly relates back to the preamble. For the method of claim 15, the preamble of the instantly claimed method is drawn to a method of expressing a heterologous peptide in a selected host cell while the final process step is that of bringing about cleavage of the suicide expression vector and it is thus unclear as to whether the instantly claimed method is drawn to method of expressing a heterologous peptide in a selected host cell, or rather bringing about cleavage of the suicide expression vector. Similarly, for the method of claim 17, the preamble of the instantly claimed method is drawn to a method of production of a microorganism vector while the final process step is that of bringing about cleavage of the suicide expression

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vector and it is thus unclear as to whether the instantly claimed method is drawn to method of production of a microorganism vector or rather bringing about cleavage of the suicide expression vector. Method claim requires a last step or phrase in the last step that states the accomplishments of the goals for the method which were stated in the method's preamble. Claims 15 and 17 lack such a last step and are confusing because the additional method step is not sufficiently set forth. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashions. See *Ex parte Erlich*, 3 USPQ2d1011, p.1011 (Bd. Pat. Applicant. Int. 1986). It is suggested that an amended claim more clearly describing the intended steps be submitted.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 2, 6, and 13-19 are rejected under 35 U.S.C. 102 (b) over Herrero et al. (Journal of Bacteriology, (1990), Vol. 172, No. 11, pages 6557-6567).

Herrero et al. teach a suicide expression vector for expressing heterologous peptide, polypeptide or protein in a selected host cell (Abstract), the vector comprising :

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(I) a first nucleotide sequence encoding the heterologous peptide, polypeptide or protein operably linked to a first promoter sequence (Figure 3, Figure 7 and Page 6500, column 1, Construction of arsenite resistance cassette subsection) ;

(ii) a second nucleotide sequence encoding a restriction enzyme (transposase) or functional portion thereof operably linked to a second promoter (lac) sequence, the second promoter sequence being inducible (Figures 2 , 3 and 7); and

(iii) one or more cleavage site(s) for the restriction enzyme or functional portion thereof, the cleavage site(s) being absent from the chromosomal DNA of the host cell (Tn5-site in Figures 2 and 7),

wherein upon introduction of the vector into the host cell, induced expression of the restriction enzyme transposase or functional portion thereof from the second nucleotide sequence brings about the cleavage of the suicide expression vector (Abstract and Figure 7).

Herrero et al. teach a suicide expression vector wherein the first nucleotide sequence encodes a protein (Figure 3, Figure 7 and Page 6500, column 1, Construction of arsenite resistance cassette subsection).

Herrero et al. teach a bacterium host cell transformed with a suicide expression vector (Abstract and Figure 9).

Herrero et al. teach a method of expressing a heterologous peptide, polypeptide or protein in a selected host cell (Abstract, Figure 3 and Results and Discussion Section), comprising:

(I) transforming the bacterium host cell with a suicide expression vector (Figure 9);

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(ii) culturing the transformed host cell under suitable conditions for the expression of the heterologous peptide, polypeptide or protein (Figure 9 and Tn5- based transposon vector delivery system, page 6562, column 2) ; and

(iii) thereafter inducing expression of the restriction enzyme or functional portion thereof to bring about the cleavage of the suicide expression vector (Abstract, Figure 3 and Results and Discussion Section).

Herrero et al. teach a method for the production of a microorganism vector which contains recombinant peptide, polypeptide or protein but no recombinant DNA (Abstract and Figure 9B), comprising:

- (I) transforming the bacterium host cell with a suicide expression vector (Figure 9B);
- (ii) culturing the transformed host cell under suitable conditions for the expression of the heterologous peptide, polypeptide or protein (Figure 9B) ; and
- (iii) thereafter inducing expression of the restriction enzyme or functional portion thereof to bring about the cleavage of the suicide expression vector (Figure 9B).

Herrero et al. teach a method wherein the microorganism is a bacterium (Abstract).

Herrero et al. teach a suicide expression vector wherein the second nucleotide sequence encodes a restriction enzyme that recognize a cleavage site(s) of ten or more nucleotides (Figure 7).

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Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 2, 6, 7, and 13-19 are rejected under 35 U.S.C. 103 (a) over Herrero et al. (Journal of Bacteriology, (1990), Vol. 172, No. 11, pages 6557-6567) in view of Marshall et al. (U.S. Patent 5,420,032) (May 30, 1995).

Herrero et al teach the suicide vector of claims 1, 2, 6, and 13-19 as described above.

Herrero et al do not teach the suicide vector wherein the second nucleotide sequence encodes a restriction enzyme selected from I-CeuI.

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Marshall et al. teach the suicide expression vector wherein a nucleotide sequence encodes a restriction enzyme selected from I-CeuI (Abstract, Figures 1-9 , Examples 1 and Columns 17-18).

Herrero et al. do not teach a suicide expression vector wherein the one or more cleavage site(s) are located at site(s) on the vector which avoids steric hindrance of binding by the restriction enzyme.

Marshall et al. teach a suicide expression vector wherein the one or more cleavage site(s) are located at site(s) on the vector which avoids steric hindrance of binding by the restriction enzyme.(Figures 1, 3 and 5).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the nucleotide sequence encoding a restriction enzyme selected from I-CeuI of Marshall et al. with the suicide expression vector of Herrero et al. since Marshall et al state, "All of the above results demonstrate that naturally occurring or synthetic substrates bearing base-pair substitutions (degenerate DNA sequence) can be recognized and cleaved by I-CeuI, a novel homing endonuclease, which will be useful as a "restriction" enzyme for cleaving low frequency sequence, because of its long recognition sequence (Column 18, lines 62-68)". Furthermore, this is also obvious that transposase gene may not be required to be integrated in the vector when transpositions are not needed in different location of the chromosomes and may be substituted with customized restriction enzyme of choice. An ordinary practitioner would have been motivated to substitute and combine the nucleotide sequence encoding a restriction enzyme selected from I-CeuI of Marshall et al. with

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the suicide expression vector of Herrero et al. , in order to achieve the express advantages, as noted by Marshall et al., of a novel homing endonuclease, which will be useful as a "restriction" enzyme for cleaving low frequency sequence, because of its long recognition sequence.

8. Claims 1, 2, 3, 6, 7, and 13-19 are rejected under 35 U.S.C. 103 (a) over Herrero et al. (Journal of Bacteriology, (1990), Vol. 172, No. 11, pages 6557-6567) in view of Hardy et al. (U.S. Patent 5,851,817) (December 22, 1998).

Herrero et al. teach suicide expression vector of claims 1, 2, 6, and 13-19 as described above.

Herrero et al. do not teach the suicide expression vector wherein the first nucleotide sequence encodes a contraceptive antigen.

Hardy et al. teach the suicide expression vector wherein the first nucleotide sequence encodes a contraceptive antigen (Abstract, Figure 10 and Example II).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the contraceptive antigen of Hardy et al. with the suicide expression vector of Herrero et al. since Hardy et al state, "Also disclosed are methods for speciating mammalian eggs, identifying species-specific sperm, and proving contraception in a mammalian population. Specifically disclosed are nucleic acid sequences and the corresponding amino acid sequences of specific sperm membrane proteins they encode, whose identification and characterization have permitted development of species-specific contraceptive and fertility compositions and methods (Abstract)". An ordinary practitioner would

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have been motivated to substitute and combine the contraceptive antigen of Hardy et al. with the suicide expression vector of Herrero et al., in order to achieve the express advantages, as noted by Hardy et al., of a specific nucleic acid sequences and the corresponding amino acid sequences of specific sperm membrane proteins they encode, whose identification and characterization have permitted development of species-specific contraceptive and fertility compositions and methods.

9. Claims 1, 2, 4, 6, 7, and 13-19 are rejected under 35 U.S.C. 103 (a) over Herrero et al. (Journal of Bacteriology, (1990), Vol. 172, No. 11, pages 6557-6567) in view of Calvet et al. (U.S. Patent 5,552,313) (September 3, 1996).

Herrero et al. et al teach suicide expression vector of claims 1, 2, 6, and 13-19 as described above.

Herrero et al. do not teach the suicide expression vector wherein the first nucleotide sequence encodes an esterase capable of hydrolyzing organophosphates.

Calvet et al. teach the suicide expression vector wherein the first nucleotide sequence encodes an esterase capable of hydrolyzing organophosphates. (Abstract, Example 12 and Column 5, line 20 to column 6, line 67).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the nucleotide sequence encoding an esterase capable of hydrolyzing organophosphates of Calvet et al. with the suicide expression vector of Herrero et al. since Calvet et al state, "Knowledge of the mouse phosphotriesterase-related sequence will permit other mammalian genes and cDNAs to be isolated by using the mouse DNA

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as a hybridization probe to screen recombinant DNA libraries from other organisms, or by using an antibody to the mouse protein to screen protein expression libraries. Having genes or cDNAs from other organisms helps in determining the protein's functions and provide better reagents for human use (column 6, lines 7-14)". An ordinary practitioner would have been motivated to substitute and combine the. nucleotide sequence encoding an esterase capable of hydrolyzing organophosphates of Calvet et al. with the suicide expression vector of Herrero et al., in order to achieve the express advantages, as noted by Calvet et al., of a knowledge of the mouse phosphotriesterase-related sequence which will permit other mammalian genes and cDNAs to be isolated by using the mouse DNA as a hybridization probe to screen recombinant DNA libraries from other organisms, or by using an antibody to the mouse protein to screen protein expression libraries.

10. Claims 1, 2, 5, 6, 7, and 13-19 are rejected under 35 U.S.C. 103 (a) over Herrero et al. (Journal of Bacteriology, (1990), Vol. 172, No. 11, pages 6557-6567) further in view of Kemp et al. (U.S. Patent 6,111,070) (August 29, 2000).

Herrero et al. teach suicide expression vector of claims 1, 2, 6, and 13-19 as described above.

Herrero et al. do not teach the suicide expression vector wherein the first nucleotide sequence encodes an insecticidal toxin.

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Kemp et al. teach the suicide expression vector wherein the first nucleotide sequence encodes an insecticidal toxin.(Abstract, Figures 1-4 and Column 13, line 37 to column 14, line 50 and Example 1).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the nucleotide sequence encoding an insecticidal toxin. of Kemp et al. with the suicide expression vector of Herrero et al. since Kemp et al state, "The introduction and expression of the structural gene for an insecticidal protein can be used to protect a crop from infestation with insect larvae of species which include, but are not limited to, hornworm, pink bollworm, European corn borer, tobacco budworm, and cabbage looper (Column 14, lines 25-31)". An ordinary practitioner would have been motivated to substitute and combine the. nucleotide sequence encoding an insecticidal toxin. of Kemp et al. with the suicide expression vector of Herrero et al., in order to achieve the express advantages, as noted by Kemp et al., of a structural gene for an insecticidal protein which can be used to protect a crop from infestation with insect larvae of species which include, but are not limited to, hornworm, pink bollworm, European corn borer, tobacco budworm, and cabbage looper.

11. Claims 1, 2, 6, 7, 9 and 13-19 are rejected under 35 U.S.C. 103 (a) over Herrero et al. (Journal of Bacteriology, (1990), Vol. 172, No. 11, pages 6557-6567) in view of Barber et al. (U.S. Patent 6,043,077) (March 28, 2000).

Herrero et al. teach suicide expression vector of claims 1, 2, 6, and 13-19 as described above.

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Herrero et al. do not teach the suicide expression vector wherein the third nucleotide sequence encodes a ribozyme targeted against specific mRNA.

Barber et al. teach the suicide expression vector wherein a nucleotide sequence encodes a ribozyme targeted against specific mRNA. (Abstract, Figures 1-3 , Examples 1-9 and Column 7, line 64 to column 8, line 16).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the nucleotide sequence encoding a ribozyme targeted against specific mRNA of Barber et al. with the suicide expression vector of Herrero et al. since Barber et al state, "These vectors provide the advantage of providing multi functional therapy against HCV infection, preferably with the various therapies working together in synergy (Column 8, lines 10-12)". An ordinary practitioner would have been motivated to substitute and combine the nucleotide sequence encoding a ribozyme targeted against specific mRNA of Barber et al. with the suicide expression vector of Herrero et al., in order to achieve the express advantages, as noted by Barber et al., of vectors which provide the advantage of providing multi functional therapy against HCV infection, preferably with the various therapies working together in synergy.

Response to Amendment

12. In view of the amendment, 112 (second paragraph) rejections regarding antecedent basis and "heterologous peptide" are hereby withdrawn. However, 112 (second paragraph) rejections

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regarding lack of final process step are hereby maintained. Moreover, claims 8-12 are objected to because they are improper multiple dependent claims. 102 (b) and other 103(a) rejections are hereby maintained.

Response to Arguments

13. Applicant's arguments filed on August 21, 2001, have been fully considered but they are not persuasive.

Applicant argues that claims 15 and 19 do not lack final process step because one of ordinary skill in the art would understand the scope of the claims. Applicant's argument is based on the assumption that "heterologous peptide, polypeptide or protein" are the same as "suicide expression vector". This assumption and the argument is not persuasive because it is well known by an ordinary practitioner in the art that "heterologous peptide, polypeptide or protein" are not necessarily synonymous and same as "suicide expression vector". Therefore, 112 (second paragraph) rejections regarding lack of final process step are hereby properly maintained.

Applicant argues that 102(b) rejection as being anticipated by Herrero et al. (Journal of Bacteriology, (1990), Vol. 172, No. 11, pages 6557-6567) should be withdrawn. This argument is not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the present invention allows expression of a suitable amount of heterologous peptide encoded by a first nucleotide sequence to accumulate in the host cell. Then, an induction agent can be used to

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cause the expression of the restriction enzyme to cleave the suicide expression vector which is then subsequently degraded in the host cell. Therefore, the present invention allows for the complete removal of the heterogeneous DNA from the host cell) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicant's arguments against the references individually to withdraw 103 (a) rejections, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant also argues that there is no motivation to combine the references. This argument is not persuasive, especially in the presence of strong motivation provided by Marshall et al, since Marshall et al. state, "All of the above results demonstrate that naturally occurring or synthetic substrates bearing base-pair substitutions (degenerate DNA sequence) can be recognized and cleaved by I-CeuI, a novel homing endonuclease, which will be useful as a "restriction" enzyme for cleaving low frequency sequence, because of its long recognition sequence (Column 18, lines 62-68)". Further explicit and strong motivation is provided by Hardy et al, since Hardy et al state, "Also disclosed are methods for speciating mammalian eggs, identifying species-specific sperm, and proving contraception in a mammalian population. Specifically disclosed are nucleic acid sequences and the corresponding amino acid sequences of specific sperm membrane

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proteins they encode, whose identification and characterization have permitted development of species-specific contraceptive and fertility compositions and methods (Abstract)". Same logic are applicable to Kemp et al and Barber et al references. Therefore, all 102 (b) as well as 103 (a) rejections are hereby properly maintained.

Conclusion

14. **THIS ACTION IS MADE FINAL** in view of the response to arguments and amendment. Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti , Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's

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supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0195.

Arun Chakrabarti,

Patent Examiner,

August 30, 2001


W. Gary Jones
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Technology Center 1600
9/6/01